

CLAIMS

We claim:

1. A method of treating hemophilia in a human comprising:
 - a) providing at least one recombinant adeno-associated virion comprising nucleotide sequences encoding Factor VIII, and
 - b) administering said at least one recombinant adeno-associated virion into said human under conditions such that said Factor VIII nucleotide sequences are expressed at a level which provides a therapeutically effective amount in said human.
2. The method of Claim 1, wherein said Factor VIII nucleotide sequences are expressed in the liver of said human.
3. The method of Claim 1, wherein said recombinant adeno-associated virion encodes the light chain of said Factor VIII.
4. The method of Claim 1, wherein said recombinant adeno-associated virion encodes the heavy chain of said Factor VIII.
5. The method of Claim 1, wherein said adeno-associated virion is administered intravenously.
6. The method of Claim 1, wherein the nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.

7. A method of treating a subject comprising:

a) providing:

- i) a subject suffering from a blood clotting disorder,
- ii) a first recombinant adeno-associated virion, comprising a nucleotide sequence encoding the light chain of Factor VIII, and
- iii) a second recombinant adeno-associated virion comprising a nucleotide sequence encoding the heavy chain of Factor VIII; and

b) administering said first and second recombinant adeno-associated virions into said subject under conditions such that said Factor VIII heavy and light chain nucleotide sequences are expressed at a level which provides a therapeutic effect in said subject.

8. The method of Claim 7, wherein said recombinant adeno-associated virion is administered intravenously.

9. The method of Claim 7, the nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.

10. A method of treating hemophilia in a mammal comprising:
- (a) providing
- i) a recombinant adeno-associated virion, wherein said recombinant adeno-associated virion comprises a nucleic acid encoding Factor VIII operably linked to an expression control element, and
- 5 ii) a mammal; and
- (b) administering an amount of said recombinant adeno-associated virion to a mammal wherein said Factor VIII is expressed at levels having a therapeutic effect on said mammal.
- 10 11. The method of Claim 10, wherein said nucleic acid encodes the light and heavy chains of Factor VIII.
12. The method of Claim 10, wherein said mammal is a human.
- 15 13. The method of Claim 10, wherein said administering comprises introducing said recombinant adeno-associated virion to the liver of said mammal.
14. The method of Claim 10, wherein said recombinant adeno-associated virion is introduced intravenously.
- 20 15. The method of Claim 14, wherein the recombinant adeno-associated virion is introduced via the portal vein.
- 25 16. The method of Claim 10, wherein said recombinant adeno-associated virion is introduced arterially.

17. The method of Claim 16, wherein said recombinant adeno-associated virion is introduced via the hepatic artery.

5 18. The method of Claim 10, wherein said nucleic acid comprises SEQ ID NO: 13.

19. The method of Claim 10, wherein said nucleic acid comprises SEQ ID NO: 14.

10 20. The method of Claim 10, wherein said expression control element is tissue-specific.

15 21. The method of Claim 10, wherein the expression control element is liver-specific.

22. The method of Claim 10, said nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.

20 23. A method of treating hemophilia A in a mammal comprising:

(a) providing:

25 i) a recombinant adeno-associated virion wherein said recombinant adeno-associated virion comprises a nucleic acid encoding a Factor VIII lacking a portion of the B-domain region and wherein said nucleic acid is operably linked to an expression control element, and

ii) a mammal suffering from hemophilia A; and

(b) administering an amount of said recombinant adeno-associated virion to a mammal wherein said Factor VIII light chain and heavy chain are expressed at levels having a therapeutic effect on said mammal.

5

24. The method of Claim 23, wherein said nucleic acid encodes the light and heavy chains of Factor VIII.

10

25. The method of Claim 23, wherein said mammal is a human.

26. The method of Claim 23, wherein said administering step comprises introducing the recombinant adeno-associated virion to the liver of said mammal.

15

27. The method of Claim 23, wherein said recombinant adeno-associated virion is introduced intravenously.

28. The method of Claim 27, wherein said recombinant adeno-associated virion is introduced via the portal vein.

20

29. The method of Claim 23, wherein said recombinant adeno-associated virion is introduced arterially.

30. The method of Claim 29, wherein said recombinant adeno-associated is introduced via the hepatic artery.

25

31. The method of Claim 23, wherein said nucleic acid comprises the Factor VIII sequence of SEQ ID NO: 13.

32. The method of Claim 23, wherein said nucleic acid comprises the Factor VIII sequence of SEQ ID NO: 14.

5 33. The method of Claim 23, wherein said expression control element is tissue-specific.

34. The method of Claim 23, wherein the expression control element is liver-specific.

10 35. The method of Claim 34, wherein said Factor VIII nucleotide sequences are expressed in the liver of said subject.

15 36. The method of Claim 23, wherein said nucleotide sequences are operably linked to tissue-specific expression control elements.

37. The method of Claim 23, wherein said nucleotide sequences are operably linked to liver-specific expression control elements.

20 38. The method of Claim 23, wherein said Factor VIII nucleotide sequences are operably linked to a tissue-specific expression control element.

39. The method of Claim 38, wherein said Factor VIII nucleotide sequences are operably linked to a liver-specific expression control element.

25 40. The method of Claim 23, said nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.